# A STUDY ON PHARMACOLOGICAL MANAGEMENT OF MIGRAINE IN A TERTIARY CARE HOSPITAL

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# ABSTRACT

## INTRODUCTION

Migraine is one of the most common recurrent types of headaches. There's no cure for migraine headaches. But many drugs can treat or even prevent them. Migraine medications used as prophylaxis in treatment of migraine includes Amitriptyline, Flunarizine, Topiramate, Propranolol, Sodium valproate, rescue medication include Rizatriptan. Magnesium plays a major role in physiological actions such as neurological functioning, cellular mechanism, most substantial evidence for magnesium's effectiveness is in patients who have or have had aura with their migraine, it is believed magnesium may prevent the wave of brain signaling, cortical spreading depression (CSD) and in platelet aggregation increase.

The assessment of migraine can be done by Migraine Therapy Assessment Questionnaire (MTAQ), a nine question migraine care management questionnaire, gathers information in five areas including symptom control, frequency of attacks, knowledge/behaviour barriers, economic burden, and overall patient satisfaction with treatment of migraine.

This prospective study conducted for six months focuses on the prevalence of usage of Amitriptyline, Flunarizine, Topiramate, Propranolol, Sodium valproate, the percentage reduction in headache frequency after using these drugs and thus the management of migraine. It also documents the percentage reduction in headache frequency in patients with and without magnesium as an add on therapy. The level of migraine control is studied using Migraine Therapy Assessment Questionnaire (MTAQ).

## AIM

To study the pharmacological management of migraine in a tertiary care hospital

## OBJECTIVES

- To document the prevalence of usage of amitriptyline, flunarizine, topiramate, propranolol and sodium valproate.

- To document the 3 month headache rate and % reduction in the headache frequency in patients after using amitryptiline, flunarizine, topiramate, propanalol and sodium valproate.
- To compare the 3 month headache rate and its % reduction in headache frequency in patients with and without magnesium as an add-on therapy.
- To document the level of migraine control using Migraine Therapy Assessment Questionnaire

## METHODOLOGY

### STUDY DESIGN

- A prospective study for a period of six months.
- Data was collected using specially designed data collection form.
- Patient were selected based on inclusion and exclusion criteria.
- The study analysed the pharmacological management of migraine.
- Data was collected by direct interaction and telephone conversation with patients and from case files in the respective department.
- This data was used to evaluate changes in migraine severity from the baseline.

### STUDY PERIOD

- A six-month study was designed using prospective data.
- The study was done by taking details of patients from the medical records and the Mediware system available in the Lourdes Hospital, Kochi and by direct and telephonic interaction for a period of 6 months.

### STUDY SETTING

This study was carried out in Neurology Department of Lourdes Hospital, Post Graduate Institute of Medical Science and Research, Ernakulam, Kochi - 682 012, Kerala, India, which is a 500 bedded multispecialty tertiary care hospital with a wide range of amenities. The institution is equipped with

7 super-specialty department and 22 other departments with facilities comprising 12 operation theatres, 10 intensive care units and a computerized Lourdes Mediware system. Clinical laboratories with ISO standards. It is one of the top most hospitals in Kerala where even the poor have access to advanced medical care in an atmosphere of love and compassion.

## STUDY POPULATION

All the patients who report with Migraine in the Neurology Department during the study period.

## SAMPLE SIZE

- ✓ As suggested by the Statistician, sample size for the study was calculated to be ≥ 138.
- ✓ The sample size was calculated by the formula,

$$n \geq \frac{Z^2 P Q}{E^2}$$

Z = 1.96, P = 10

- ✓ Where n is the sample size, Z is the statistic corresponding to level of confidence (95%)
- ✓ P is expected prevalence, E is the allowable error 5%.

## METHOD OF SELECTION

Patients were selected based on inclusion and exclusion criteria.

## INCLUSION CRITERA

- Classification of migraine according to ICHD
- All genders are eligible
- Patients taking Amitriptyline, topiramate, flunarizine, propranolol, and sodium valproate

## EXCLUSION CRITERIA

- Incomplete data.
- Patients not willing to participate.

## DATA COLLECTION

The data were collected using specially designed data collection form. Prospective patient demographic details as well as treatment details were extracted from medical records and Lourdes Mediware system and the follow up was done by telecommunication.

## DATA COLLECTION TOOL

- Medical records and Lourdes Mediware system.
- Specially designed data collection forms.
- Migraine Therapy Assessment Questionnaire (MTAQ).

## DATA COLLECTION METHOD

Details of patient with migraine (during a period of 6 months November 2022- April 2023) were collected from the medical records and the Medi-ware system available in Lourdes Hospital, Kochi. The selected cases were then analysed by obtaining those files from medical records department and subsequently entered into data collection forms. The collected data were verified before entering on the terms of inclusion and exclusion criteria. The follow up was carried out using MTAQ through telecommunication. The data was entered into Microsoft excel and further analysis done using SPSS statistical software.

## STATISTICAL ANALYSIS

The collected data were compiled using Microsoft Excel and were presented using tables and graphs. The data were tabulated, analyzed and compared with relevant studies. Analyses were carried out at 5% level of statistical significance. The statistical software SPSS was used for analysis of the data. One-way ANOVA test, MacNemar $\chi 2$ test and, Paired samples t-test were the tests used in the procedure.

## RESULTS AND DISCUSSION

A total of 154 patients having migraine was studied during the study period. The study deduced that patients of age between 40 and 50 years had higher prevalence of migraine f= (25) (16.23%)_and the female population is more affected by migraine (f= (107) (69%). The study also concluded that migraine with aura is more prevalent in migraine patients (f=127)82.5% in contrast to previous studies. In the study setup migraine with bilateral origin was more prevalent than unilateral origin.

It was found that the most prescribed medication in the study setting was amitriptyline f =95(61.7%) followed by topiramate and flunarizine. The average percentage reduction in migraine attack frequency when using the different drugs was studied and it was found that among the 5 drugs under study flunarizine showed higher average percentage reduction in 3 months migraine frequency (62.086%) Magnesium supplement given as an add-on therapy recorded 65.153% average percentage reduction in migraine attack frequency, concluding that magnesium as an add on therapy improves the results of the management. According to the managemental issue breakdown using the Migraine Therapy Assessment Questionnaire; Poor symptom control and high attack frequency were the most common managemental issues, and were resolved in the follow-up research,

## CONCLUSION

Our study aimed at better understanding of migraine and its management. The study found that amitriptyline was the most commonly used prophylactic medicine in the management of migraine in the study setting and also found out that magnesium as an add-on improves the overall migraine control. The Migraine Therapy Assessment Questionnaire identified that the most prevalent management issue was poor symptom control and high attack frequency and also recorded decline in the frequency of attacks and emergency visits indicating better migraine control at the follow up month.

# INTRODUCTION

## HEADACHE IN ANCIENT TIMES

The history of headache and neuroscience goes as early as 7000 BC, when the signs of ancient neurosurgery were evident. Neolithic skulls show that trepanation (the removal of a segment of bone from the skull) was widely performed. Trepanning was still recommended by some 17th century physicians for the treatment of migraine. In 1660, William Harvey recommended trepanation to a patient with intractable migraine.

The Ebers Papyrus, dating back to about 1200BC and named after a professor of Egyptology, mentions migraine, neuralgia, and shooting head pains, and is said to be based on earlier medical documents from around 1550BC. Following the instructions on the papyrus, the Egyptians would firmly bind a clay crocodile holding grain in its mouth to the head of the patient using a strip of linen. The linen bore the names of the gods whom the Egyptians believed could cure their ailments. In actual fact, the process may have relieved the headache by compressing the scalp, and possibly collapsing distended vessels that were causing the pain.

ANCIENT GREEK AND ROMAN SCHOLARS

Hippocrates – in 400 BC – was the first to describe visual symptoms of migraine. He described a shining light, usually in the right eye, followed by violent pain beginning in the temples and eventually reaching the entire head and neck area.

Headaches have long been attributed to digestive disturbances and to the flow of bile, one of the digestive juices. Almost 2,000 years ago the Roman physician Galen commented: "*How constantly do we see the head attacked with pain when yellow bile is contained in the stomach: as also the pain forthwith ceasing when the bile has been vomited.*" Hippocrates, attributing migraine to vapors rising from the stomach to the head, realized that vomiting, when possible, could partially relieve the pain of headache. The vomiting attacks of childhood, often migrainous in nature, are still referred to as "bilious attacks".

## HEADACHE IN MIDDLE AGE

In 1098-1180 Hildegard of Bingen wrote about her 'visions' which were thought to be migraine aura. European headache treatments in the Middle Ages involved drugs- soaked poultices and opium and vinegar solutions.

## THE SCIENTIFIC ERA

In 1672 Thomas Willis introduces the term 'neurology' and the vascular theory of headache, in 1770s Erasmus Darwin proposed centrifugation as a treatment, in 1873 Edward Liveing published his first major work devoted to migraine and introduced the theory of nervous system dysfunction. In 1888 William Gowers published influential textbook on neurology. He also divided headache treatment into acute and preventive.

## THE 20TH CENTURY

In 1908 Paul Ehlich won Nobel Prize for work on receptors in the brain. In 1930s Harold Wolffe studied headache in the laboratory, performing many laboratory experiments which supported the vascular theory of headache. In 1960s research into migraine and headache began at The Prince Henry and Prince of Wales hospitals in Sydney. Late 1960s serotonin is found to treat headache, but it had too many side effects. In 1972-1990 Dr. Patrick Humphrey in the UK built on this research to develop triptans. [1]

## WHAT IS MIGRAINE?

Migraine is one of the most common recurrent types of headaches. This neurological disorder is characterized by pain in head most often unilateral and generally associated with nausea and vomiting, various other symptoms may include photophobia, phonophobia and sometimes visual sensory disorders such as zigzag vision, flashes of light, language/speech turbulences, sensory, and motor abnormalities. Aura is a transitory focal neurological discrepancy characterized by visual language/speech, sensory, or motor anomalies. [4]

### Migraine Symptoms

Migraine is different in everyone. In many people, it happens in stages. These stages may include:

1. **Prodrome**

Hours or days before a headache, about 60% of people who have migraine notice symptoms like:

- Being sensitive to light, sound, or smell
- Fatigue
- Food cravings or lack of appetite

- Mood changes
- Severe thirst
- Bloating
- Constipation or diarrhea.

2. **Aura**

These symptoms stem from the nervous system and often involve our vision. They usually start gradually, over a 5- to 20-minute period, and last less than an hour. Symptoms include:

- Seeing black dots, wavy lines, flashes of light, or hallucinations
- Have tunnel vision
- Blind spots
- Have tingling or numbness on one side of the body
- Having trouble speaking clearly
- Have a heavy feeling in the arms and legs
- Have ringing like sensation in the ears

3. **Attack**

A migraine headache often begins as a dull ache and grows into throbbing pain. It usually gets worse during physical activity. The pain can move from one side of the head to the other, it can be in the front of the head, or one can feel like it's affecting the entire head.

About 80% of people have nausea along with a headache, and about half vomit. The person may also appear to be pale and clammy or faint.

Most migraine headaches last about 4 hours, but severe ones can go for more than 3 days. It's common to get two to four headaches per month. Some people may get migraine headaches every few days, while others get them once or twice a year.

4. **Postdrome**

This stage can last up to a day after a headache. Symptoms include:

- Feeling tired, wiped out, or cranky
- Feeling unusually refreshed or happy
- Muscle pain or weakness
- Food cravings or lack of appetite

Migraine Causes

The exact cause of migraine headaches is unknown, although it seems to be related to changes in the brain and in the genes. Migraine may be passed down from one's parents. For many years, scientists thought migraine happened because of changes in blood flow in the brain.

Current thinking is that a migraine likely starts when overactive nerve cells send out signals that trigger the trigeminal nerve, which gives sensation to the head and face. This cues our body to release chemicals like serotonin and calcitonin gene-related peptide (CGRP). CGRP makes blood vessels in the lining of brain swell. Then, neurotransmitters cause inflammation and pain. [1], [4]

Migraine Risk Factors

The American Migraine Foundation estimates that more than 38 million Americans get migraines. Migraine risk factors includes:

- **Sex:** Women have migraines three times more often than men.
- **Age:** Most people start having migraine headaches between ages 10 and 40. But many women find that their migraines get better or go away after age 50.
- **Family history:** Four out of five people with migraine have other family members who get them. If one parent has a history of these types of headaches, their child has a 50% chance of getting them. If both parents have them, the risk raises to 75%.
- **Other medical conditions include:** Depression, anxiety, bipolar disorder, sleep disorders, and epilepsy. [4]

**Migraine Triggers**

Some common migraine triggers include:

- Hormone changes: Many women have headaches around their period, while they're pregnant, or when they are ovulating. Symptoms may also be tied to menopause, birth control that uses hormones, or hormone replacement therapy.
- Stress: Brain releases chemicals that can cause blood vessel changes that might lead to a migraine.
- Foods: Some foods and drinks, such as aged cheese, alcohol, and food additives like nitrates and monosodium glutamate (MSG), cause migraine.
- Skipping meals

- Caffeine: Getting too much or not getting as much as caffeine may cause headaches. Caffeine itself can be a treatment for acute migraine attacks.
- Changes in weather: Storm fronts, changes in barometric pressure, strong winds, or changes in altitude can all trigger a migraine.
- Senses: Loud noises, bright lights, and strong smells can set off a migraine.
- Medications: Vasodilators, which widen blood vessels, can trigger them.
- Physical activity: This includes exercise and sex.
- Tobacco
- Changes in sleep: Too much or not enough sleep. [4]

Migraine Types

- There are several kinds of migraines. The most common are **migraine without aura** (or common migraine) and **migraine with aura** (also known as a classic migraine).
- 1) Migraine without aura, is a clinical syndrome characterized by headache with special features and associated symptoms. 2) Migraine with aura, is primarily characterized by transient focal neurological symptoms that usually precede or sometimes accompany the headache that is experienced in almost one-third of patients. Some patients also experience a prodromal phase, occurring hours or days before the headache, and/or a postdromal phase following headache resolution. Prodromal and postdromal symptoms include hyperactivity, hypo-activity, and depression, cravings for particular foods, repetitive yawning, fatigue and neck stiffness and/or pain.

Other types include:

- **Menstrual migraine:** This is when the headache is linked to period. These usually happen 2 days before period starts and last through 3 days after. Other kinds of migraine headaches may occur during the month, but the migraine around menstruation is usually without aura.
- **Silent migraine:** This kind is also known as an acephalgic migraine. The symptoms are similar to that of migraine with aura. In fact, aura is usually the main warning sign of this type of migraine. But nausea and other migraine symptoms may also occur. It usually lasts only about 20-30 minutes.
- **Vestibular migraine:** Symptoms include balance problems, vertigo, nausea, and vomiting, with or without a headache. This kind usually happens in people who have a history of motion sickness.

- **Abdominal migraine:** It causes stomach pain, nausea, and vomiting. It often happens in children and may change into classic migraine headaches over time.
- **Hemiplegic migraine:** It causes a short period of paralysis (hemiplegia) or weakness on one side of the body. Symptoms may include numbness, dizziness, or vision changes.
- **Ocular migraine:** This is also known as an ophthalmic or retinal migraine. It causes short-lived, partial, or total loss of vision in one eye, along with a dull ache behind the eye, which may spread to the rest of the head.
- **Migraine with brainstem aura:** Dizziness, confusion, or loss of balance can happen before the headache. The pain may affect the back of the head. These symptoms usually start suddenly and can come along with trouble speaking, ringing sensation in ears, and vomiting. This type of migraine is strongly linked to hormone changes and mainly affects young adult women.
- **Status migrainosus:** This severe type of migraine can last more than 72 hours. The pain and nausea may be intense. Sometimes, medicines or medication withdrawal can cause them.
- **Ophthalmologic migraine:** This causes pain around the eye, including paralysis of the muscles around it. This is a medical emergency because the symptoms can also be caused by pressure on the nerves behind the eye or by an aneurysm. Other symptoms include a droopy eyelid, double vision, or other vision changes. [3]

Migraine Frequency

Migraine frequencies may be divided into three. Episodic migraine means one gets the migraine often. High-frequency episodic migraine means one will have 8 to 14 migraine headache days per month. This condition is more likely to develop into chronic migraine.

Chronic migraine means migraine headaches more than 15 days in a month and eight of those days have migraine features such as:

- Moderate to intense head pain
- Pain is on side of head (one or both)
- Pain throbs or pulsates
- Pain gets worse on moving
- Nausea or vomiting
- Sensitive to light and sound

The current estimate of global migraine prevalence is 14-15% and the one-year prevalence of migraine in India was 25.6%.

Chronic and even high-frequency episodic migraine can cause disabling conditions. And the higher the pain intensity of each headache, the more disabling it can be.

Migraine Diagnosis

It is diagnosed on the basis of signs and symptoms, which includes

- Location of onset of pain
- Frequency of attacks
- Duration of pain
- Other family members who have migraine
- All the medicines and supplements consumed, even over-the-counter medications.

The tests to rule out other things that could cause your symptoms, includes:

- Blood tests
- Imaging tests like MRI or CT scans
- Electroencephalogram (EEG) [1]

MIGRAINE TREATMENT

Migraine headaches have no cure. But many drugs can treat or even prevent them.

**Preventive medicines:** In case of severe headaches, four or more migraine days a month or if the treatment doesn't work, preventive medicines are prescribed. One should take them regularly to make the headaches less severe or frequent.

They include seizure medicines i.e. anticonvulsant drugs like topiramate, valproate, zonisamide. Side effects of anticonvulsants may include nausea, vomiting, diarrhoea, weight gain, sleepiness, dizziness, blurred vision ; blood pressure medicines like beta-blockers like propranolol, atenolol, timolol, metoprolol, nadolol, side effects of beta-blockers may include fatigue, nausea, dizziness when standing, and depression, insomnia and calcium channel blockers like diltiazem, nimodipine, and verapamil, side effects of calcium channel blockers may include low blood pressure, weight gain, dizziness, constipation, some antidepressants, and shots of botulinum toxin type A (Botox). [5]

Migraine medications used as prophylaxis in treatment of migraine includes:

1) Amitriptyline

This drug belongs to class tricyclic antidepressants, also shows analgesic properties. It is used to treat neuropathic pain and depression and as prophylactic treatment of migraine in adults. Off label uses include irritable bowel syndrome, sleep disorders, diabetic neuropathy, agitation, fibromyalgia and insomnia.

Mechanism of action: it acts by inhibiting the membrane pump mechanism responsible for the reuptake of transmitter amines such as norepinephrine and serotonin, thereby increasing their concentration at the synaptic clefts of the brain. [6]

2) Flunarizine

This drug belongs to class 4 calcium antagonists, a selective calcium entry blocker with calmodulin binding properties and histamine H-1 blocking properties used as migraine prophylaxis in patients with severe and frequent episodes who have not responded adequately to more common treatments.

Mechanism of action: it acts by inhibiting the influx of extracellular calcium through myocardial and vascular membrane pores by physically plugging the channel. The reduction in intracellular calcium inhibits the contractile processes of smooth muscle cells, causing dilation of the coronary and systemic arteries, increased oxygen delivery to the myocardial tissue, decreased total peripheral resistance, and systemic blood pressure and after load reductions. [9]

3) Topiramate

This drug belongs to the class second generation antiepileptic drugs used in the control of epilepsy and in the prophylaxis and treatment of migraines. Off label uses include adjunct therapy for weight management and for mood disorders.

Mechanism of action: Topiramate stimulates GABA-A receptor activity at brain non-benzodiazepine receptor sites and reduces glutamate activity at both AMPA and kinase receptors. Normally, GABA-A receptors are stimulatory for neuronal activity. By increasing GABA activity and inhibiting glutamate activity, topiramate blocks neuronal excitability, preventing seizures and migraines. Additionally it blocks the voltage-dependent sodium channels, further blocking seizure activity and carbonic anhydrase isoenzymes. [7, 8]

4) Propranolol

This drug belongs to class non selective beta-adrenergic antagonists used to treat hypertension, angina, atrial fibrillation, myocardial infarction, migraine, essential tremor, hypertrophic subaortic stenosis, and pheochromocytoma.

Mechanism of action: it acts by blocking the receptors leading to vasoconstriction, also acts by inhibition of angiogenic factors like vascular endothelial growth factor (VEGF) and basic growth factor of fibroblasts (bFGF), induction of apoptosis of endothelial cells, as well as down regulation of renin-angiotensin-aldosterone system ( RAAS). [10]

5) Sodium valproate

This drug belongs to the class anticonvulsants and are used to control complex partial seizures and both simple and complex absence seizures, bipolar disorder and occasionally used to prevent migraine headaches. The off-label uses may include treatment of acute bipolar depression, emergency treatment of status epilepticus.

Mechanism of action: it exhibits pharmacological effects by acting on GABA levels in the CNS, blocking voltage-gated ion channels, and inhibiting histone deacetylase. Impaired GABAergic inhibitory activity is established and the pathophysiology of seizure initiation and propagation, given that controlling this pathway a potential target for antiepileptic drugs.

**Rescue medication** include

Rizatriptan

This drug belongs to class second generation triptan and a selective 5-HT receptor antagonist used in the rescue treatment of migraine.

Mechanism of action: it acts on 5-HT 1B and 5-HT 1D receptors on intracranial blood pressures and sensory nerves of the trigeminal system. It binds to these receptors with high affinity. It also causes vasoconstriction of intracranial extracerebral blood vessels, which is thought to occur primarily via 5-HT 1B receptors.

Acute treatment, for pain and other symptoms during a migraine headache. Preventive treatment, to reduce the frequency and severity of migraines

Common migraine treatments include:

- Pain Killers (for pain relief).

Some over-the-counter (OTC) painkillers are commonly used for migraines, but many are only available in prescription strength.

Aside from acetaminophen, an analgesic that only relieves pain, these drugs are nonsteroidal anti-inflammatory drugs (NSAIDS), which relieve pain and reduce inflammation:

- Acetaminophen
- Aspirin
- Diclofenac
- Ibuprofen
- Ketorolac
- Naproxen

Excessive use of these medications can cause rebound headaches or addiction. Clinicians may suggest prescription medicines that may work well to end the migraine pain, including triptans, as well as the newer ditans and gepants.

Possible side effects of long-term NSAID use include:

- Heart attack
- Stroke
- Kidney damage
- Stomach ulcers

Triptans

Triptans are a newer class of drug that increases serotonin levels in your brain, reducing inflammation and constricting blood vessels, effectively ending a migraine. Triptans are available as pills, nasal sprays, injections, and tablets that dissolve under the tongue, and work quickly to stop a migraine. These drugs balance the chemicals in your brain. Examples- rizatriptan, almotriptan, eletriptan, sumatriptan, and zolmitriptan.

Ergotamine

This also works on the chemicals in brain. Ergotamines were the first class of drugs used specially for migraines. They cause blood vessels around the brain to contract and can relieve a migraine within a few minutes. Ergotamines are available as pills, tablets that dissolve under the tongue, nasal sprays, suppositories, and injections. They're generally taken at the first sign of headache symptoms, and some have the option to take additional doses every 30 minutes if the headache continues.

Some ergotamines are:

- Dihydroergotamine
- Ergotamine
- Ergotamine And Caffeine
- Methysergide
- Methylergonovine

Ergotamines can have dangerous side effects. They can cause birth defects and heart problems, and are toxic in high doses.

In pregnant or breastfeeding or heart disease patients, one shouldn't take ergotamines. Ergotamines can also interact negatively with other drugs, including antifungal and antibiotic medication.

Antinausea drugs:

These drugs reduce nausea and vomiting that can accompany severe migraines. They're usually taken along with a painkiller, as they don't reduce pain.

Some include:

- Dimenhydrinate
- Metoclopramide
- Prochlorperazine
- Promethazine
- Trimethobenzamide

These drugs may cause drowsiness, less alert, or dizzy, and have other possible side effects.

- Lasmiditan: This drug eases pain, nausea, and sensitivity to light or sound.
- Opioids: These are much powerful painkillers. Many migraine drugs are a combination of opioids and painkillers. Some opioids are:
- Codeine
- Meperidine
- Morphine
- Oxycodone

Opioids carry a serious risk of addiction, so they're usually prescribed sparingly.

- **CGRP receptor antagonists.** CGRP antagonists are the newest group of medications approved for prevention of migraines.

They work on the calcitonin gene-related peptide (CGRP), a protein that found around the brain. CGRP is involved in the pain associated with a migraine.

This class of medications is expected to grow over the coming years. Current ones include:

- Erenumab
- Fremanezumab [2]
- **Single-pulse transcranial magnetic stimulation (sTMS):** This device is palced on the back of the head at the start of a migraine with aura. It sends a pulse of magnetic energy to part of the brain, which may stop or reduce pain.
- **Neuromodulation devices:** Other devices can affect the vagus nerve and the trigeminal nerve to give relief from or prevent migraine.

**Home remedies**

Migraine can be relieved by

- Resting with eyes closed in a dark, quiet room
- Putting a cool compress or ice pack on the forehead
- Drinking plenty of liquids

**Complementary and alternative treatments**

Some people get relief with therapies they use in addition to or instead of traditional medical treatment. These are called complementary or alternative treatments. For migraine, they include:

- **Biofeedback:** This helps one to take notes of stressful situations that could trigger symptoms. If the headache begins slowly, biofeedback can stop the attack before it becomes full-blown.
- **Cognitive behavioral therapy (CBT):** A specialist can teach you how actions and thoughts affect how you sense pain.
- **Supplements:** Research has found that some vitamins, minerals, and herbs can prevent or treat migraine. These include riboflavin, coenzyme Q10, and melatonin. Butterbur may head off migraine, but it can also affect liver enzymes.
- **Body work:** Physical treatments like chiropractic, massage, acupressure, acupuncture, and craniosacral therapy might ease headache symptoms.

Migraine Prevention

- Identify and avoid triggers: Keep track of the symptom patterns in a diary so that it will be easy to figure out what's causing them.
- Manage stress: Relaxation techniques like meditation, yoga, and mindful breathing.

- Eat on a regular schedule.
- Drink lots of fluids.
- Get plenty of rest.
- Regular moderate exercise.
- Preventive medicines.

## ROLE OF MAGNESIUM IN MIGRAINE PATHOPHYSIOLOGY

As the second most abundant intracellular cation, magnesium plays a pivotal role in the physiology of the human body. It plays a major role in physiological actions such as neurological functioning, cellular mechanism, it also plays an important role in the platelet aggregation increase and in the pathophysiology of migraine as it governs the cortical spreading depression which is an underlying mechanism of migraine attack.

Routine blood test do not reflect true body magnesium source since less than 2% is in the measurable, extracellular space, 67% is in the bone and 31% is located in the intra-cellular space. An example that empirically supports this is the clinical trial by Bigal et al in which administration of 1000 mg magnesium sulfate in migraineurs with aura led to a significant improvement of pain and all the other associated symptoms that were monitored.

Magnesium in its ionized form may also effect the functioning of several other neurotransmitters such as serotonin, and pre-treatment with magnesium prevent the vasoconstriction produced by magnesium in a safer and cheaper way, potentiating the advantage and impact of magnesium in the prevention of migraine. The most substantial evidence for magnesium's effectiveness is in patients who have or have had aura with their migraine.

It is believed magnesium may prevent the wave of brain signalling, cortical spreading depression (CSD) and in platelet aggregation increase. This ion is a crucial cofactor for more than 350 enzymes particularly those necessitating adenosine triphosphate (ATP) to be fully functional including the numerous protein kinases, proteins contributed to nucleic acid metabolism or ATP-ases involved in various ions transportation.

Magnesium balance in the body is mainly regulated through renal reabsorption and gastrointestinal absorption. Altered gastrointestinal absorption can cause negative body Mg balance. Mg deficiency is normally specified by measuring serum Mg concentrations which are placed between 0.7 and 1.05 mmol/L in healthy individuals. The spreading depression (SD) is specified by the

breakdown of ion homeostasis is related to a temporary cessation of neuronal function, and is understood to play role in migraine pathogenesis and needs the release of glutamate. N-methyl-D-aspartate (NMDA) receptors play a critical role in the propagation of this procedure.

Previous investigations have reported that by confirmation of magnetic resonance spectroscopy (MRS) in brain, the decreased levels of Mg in serum, saliva, and cerebrospinal fluid (CSF) of migraine patients are obvious during and between migraine attacks. Mg deficiency influences the neuro-inflammation, serotonin 3 receptor affinity, NMDA receptor blockage, calcium channel, and glutamate and nitric oxide activity.

Magnesium counteracts both vascular and neurogenic mechanisms of migraine. The ideal medication for the prevention and treatment of migraine would have no side effects, no effects, and no risk, would be safe in pregnancy, as well as be highly effective while remaining inexpensive. Of-course no such medications exists, but magnesium comes closer than many interventions on all these fronts. Magnesium oxide is frequently used in pill form to prevent migraine, usually at a dose of 400-600 mg per day. Acutely, it can be dosed in pill form at the same dosage or given intravenously as magnesium sulfate at 1-2 gm.

The most frequent side effect is diarrhea which can be helpful in those prone to constipation. Diarrhea and abdominal cramping that is sometimes experienced is dose-responsive, such that a lower dose or decreasing the frequency of intake usually take cares of the problem. Magnesium oxide in doses up to 400 mg is pregnancy category A, which means it can be safely in pregnancy.

Many possible migraine triggers have been suggested, including hormonal (estrogen), emotional (stress, anxiety, tension), physical (tiredness, poor- quality sleep), dietary (missed, delayed or irregular meals, dehydration, alcohol), environmental (bright lights, flickering screens, loud noises) and medicinal (sedatives, combined oral contraceptive pill, HRT) factors. Migraine is a genetically influenced complex disorder. It is estimated that up to 60% of people get migraine because of their genes. These genes make people more sensitive to changes in their environment such as lifestyle factors and triggers that can bring on an attack. [11]

A number of genes are involved and there's susceptibility in those genes. This is referred to as an 'association' meaning if there is a particular gene variation, then one is more likely to suffer from the disorder. Some other types of migraine are caused by mutations in specific. There are three identified causal genes found in Hemiplegic Migraine – CACNA1A, ATP1A2 and SCN1A. [11]

Migraine being one of the most prevalent diseases in this era is still being underdiagnosed because of several reasons. To study the different issues in the management of migraine. The **MTAQ** is a useful tool.

## MIGRAINE THERAPY ASSESSMENT QUESTIONNAIRE

The assessment of migraine can be done by Migraine Therapy Assessment Questionnaire (MTAQ), which is a reliable and valid questionnaire to identify migraineurs whose migraine management maybe suboptimal in a primary care setting, it also assesses the level of migraine control for pre/post measurement.

The MTAQ is a brief survey designed to identify possible management issues for patients with migraine. The MTAQ consists of nine dichotomously scaled questions that focus on migraine control, frequency of attacks, knowledge and behavioral barriers, economic burden, and treatment satisfaction.

Each MTAQ questions receives a score based on the response categories.1 for yes and 0 for no answers. Questions 1, 2, 5, and 9 being reverse coded receives yes0, no1.

And questions 3 and 4 are scored together.

- If questions 3 and 4 are yes responses, then together their score is 0
- If question 3 has a no response and question 4 has either a yes or no response, the combined score will also be 0.
- If question 3 has a yes response and question 4 has a no response, then their combined score will be 1

This yields a total MTAQ score ranging from 0 to 8. A higher score indicating a greater number of migraine management issues. The individual MTAQ questions can be combined to form three broader domains: migraine control, knowledge/ behaviour /treatment satisfaction, and economic burden. The MTAQ is appropriate for use with individuals having a reading level of fifth grade or higher.

1. Management issue 1: Poor symptom control, included MTAQ questions 1 and 2.
2. Management issue 2: High attack frequency, included MTAQ questions 3 and 4.
3. Management issue 3: Knowledge/ behavioral barrier, included MTAQ questions 5 and 6.
4. Management issue 4: Economic burden, included MTAQ questions 7 and 8.

5. Management issue 5: Dissatisfaction with treatment, included MTAQ question 9. [12]

Despite having a high incidence of 25.2%, migraines are still incurable, and their consequences and overall burden are growing at an alarming rate. Understanding the causes and problems preventing effective migraine care is essential, as is learning about novel migraine preventative drug options that can help.